bizarre 'polymyositis', with bizarre disruptive changes in enzyme distribution in the muscle fibres.

National inquiry into convulsive disorders in childhood. Euan M. Ross (*introduced by Dr. Peter M. Dunn*) (*Department of Child Health, University of Bristol*). A detailed study is being made of the incidence, nature, and pattern of convulsive disorders reported in the 15,000 surviving children born in England, Scotland, and Wales during the week 3-9 March 1958, and originally included in the Perinatal Mortality Study. 89% of these children were traced and studied as the National Child Development Study (1958 cohort).

As a result of comprehensive medical, social, and educational studies made when the children were aged 7 and repeated at age 11, it was possible to select 1100 children who had been reported as having had one or more convulsions, faints, or breath-holding episodes. From an exhaustive study of individual records it was possible to identify 347 children who fulfilled one or more of the following: (1) History of anticonvulsant medication. (2) Had had an EEG. (3) Regarded by a doctor as being 'epileptic'. (4) Had one or more definite seizures after age 5. (5) Had had three definite seizures at some time. (6) Teacher reported a seizure at school. (7) One or more seizures reported but also attends a special school.

Precoded questionnaires were sent to both the practitioners and consultants and, in certain cases, local authority doctors, who had looked after these children. To date there has been a 95% reply rate. In 98 children (6.3 per 1000) a doctor has at some stage regarded the child as being 'epileptic'. Only 32 children however, have had one or more fits since age 8 years (2 per 1000). Only 2 children appeared to have uncomplicated *petit mal* though a further 9 had mixed *petit* and *grand mal*. Patterns of drug administration were briefly described.

REFERENCE

- Davie, R., Butler, N., and Goldstein, H. (1972). *From Birth to Seven Years*. Longmans, London.

Substrate induction of galactokinase in cultured fibroblasts from subjects heterozygous and homozygous for galactokinase deficiency. F. Zaccello, P. F. Benson, P. Croll, F. Giannelli, and T. P. Mann (*Paediatric Research Unit, Guy's Hospital Medical School, London S.E.1*). Skin fibroblasts from a patient with galactokinase deficiency (Cook, Don, and Mann, 1971), the parents, and 4 controls were cultured in minimum essential Eagle's medium containing 10% human serum, either without or with galactose (5 or 15 mg/100 ml culture medium). Fibroblasts were harvested and assayed for galactokinase activity at intervals during a 15-day period, during which time the cells were trypsinized approximately every 7 days and the medium was changed every 3 days.

Mean galactokinase activity for normal fibroblasts was 6.18 units (n moles of galactose 1-phosphate

formed/hr per mg fibroblast protein) without galactose in the medium. In the presence of galactose, activity was induced by the 3rd day, reached a maximum by the 6th day, and remained at the induced level until the 15th day. Mean activities were 9.45 units (with galactose 5 mg/100 ml) and 9.97 units (with galactose 15 mg/100 ml).

The patient with galactokinase deficiency had activities of 0.26 and 0.38 units without and with galactose in the medium (15 mg/100 ml), respectively. The father had a mean galactokinase activity of 3.20 units (51.8% of control) and the mother 2.68 units (43.4% of control). Mean activities in the presence of galactose (15 mg/100 ml) were: father 4.10 units (43.8% of control), mother 3.00 units (32.0% of control).

Fibroblast galactokinase thus has properties both of a constitutive enzyme (since it is present in cells cultured in a medium without substrate) and of a substrate inducible enzyme. Galactokinase activity in heterozygous cells was intermediate between that of cells that were homozygous normal and those that were homozygous for galactokinase deficiency. Both in the induced and uninduced states, galactokinase activities were higher in the father (43.8% and 51.8% of control values respectively) than in the mother (32.0% and 43.4% of control values respectively).

REFERENCE

- Cook, J. G. H., Don, N. A., and Mann, T. P. (1971). Hereditary galactokinase deficiency. *Archives of Disease in Childhood* 46, 465.

Plasma levels of cystine in homocystinuria. I. B. Sardharwalla and B. Fowler (*Willink Biochemical Genetics Laboratory, Royal Manchester Children's Hospital, Pendlebury, Manchester*). In homocystinuria plasma levels of cyst(e)ine are low; one explanation for this finding is the lack of methionine conversion to cysteine. It is probable that there is a different and perhaps more significant reason for the reduced concentrations of cyst(e)ine. In this paper results of two studies are presented to expound the latter view.

In the first, a 7-year-old pyridoxine-resistant patient was given (1) low methionine diet followed by (2) high methionine diet (by adding L-methionine to the basic diet) to which (3) betaine hydrochloride was then added. Throughout the study, dietary cystine was kept constant. Measurements of sulphur amino acids in the plasma and urine were performed by ion exchange chromatography, the column effluent being simultaneously monitored with ninhydrin and iodoplatinate analytical systems. The results showed that (1) there was a reciprocal relation between the plasma levels of homocyst(e)ine and cyst(e)ine, and (2) cyst(e)ine was increased in spite of very high levels of methionine during betaine therapy.

In the second study, cysteine loads were given to a 21-year-old pyridoxine-resistant patient (1) before and (2) during betaine therapy while the patient was on a constant normal diet. The result showed that on a fixed normal diet plasma levels of homocysteine-cysteine-disulphide increased significantly and there was a

considerable increase in the excretion of certain unidentified iodoplatinate reacting compounds in the first 6-hour urine. When plasma homocyst(e)ine level was high, cyst(e)ine levels after the load were significantly lower than those when homocyst(e)ine was much reduced following administration of betaine.

The results suggest that when plasma homocyst(e)ine and methionine are raised, the low levels of cyst(e)ine are due to the incorporation of a very significant proportion of dietary cyst(e)ine into homocysteine-cysteine-disulphide and other sulphur compounds (as yet unidentified) which are derived from homocyst(e)ine or methionine.

Temporary tyrosinosis. Douglas Pickering and Brian Bower (*Radcliffe Infirmary Oxford*). A term baby started to vomit at 4 weeks of age and on admission one week later was in hepatocellular failure with haemorrhage from hypoprothrombinaemia. Large amounts of tyrosine in the urine led to the diagnosis of tyrosinosis and treatment with a low phenylalanine, low tyrosine diet for 15 months (though increasing amounts of tyrosine had been introduced towards the end of the period). Initial complications were (1) oedema from hypoalbuminaemia, (2) drowsiness and apathy from hypermethioninaemia after starting the diet, and later (3) failure to gain weight due to a too drastic tyrosine reduction.

The special diet was finally abandoned at the age of 16 months with no complications. When last seen at 3 years 4 months he was normal.

A subsequent sib showed no clinical or biochemical features of tyrosinosis.

Urinary excretion of immunoglobulin E. T. M. Barratt, M. W. Turner, and S. G. O. Johansson (*Department of Immunology, Institute of Child Health, London W.C.1, and The Blood Centre, University Hospital, Uppsala, Sweden*). Immunoglobulin E (IgE) was measured by the radioimmunosorbent technique in sera and urine concentrates of healthy individuals. The urine: plasma ratio of IgE exceeded that of albumin about thirtyfold. As IgE is a considerably larger molecule and would not be expected to cross the glomerular basement as easily as albumin, the data suggest that most urinary IgE does not derive from glomerular filtration but is of local origin within the urinary tract.

If this were so, the urinary excretion of IgE would be independent of the plasma IgE concentration and perhaps also of the alterations in glomerular permeability of the nephrotic syndrome. Urinary IgE excretion rates were therefore measured in individuals with the nephrotic syndrome and in patients with atopic eczema characterized by the very high levels of plasma IgE. The results did not differ from those observed in healthy individuals, and provide further support for the hypothesis that most urinary IgE is locally secreted.

Maintenance of breathing in newborn lamb. P. Johnson, G. S. Dawes, and J. S. Robinson (*introduced by P. M. Dunn*) (*Nuffield Institute for Medical*

Research, Oxford). It has been considered by many that the immersion of the fetus in liquid inhibits respiration. Our experiments show that the fetal lamb with a tracheostomy can establish respiration and that the newborn lamb will maintain respiration when immersed in normal saline but not in water. Likewise in 8 newborn Cheviot lambs under 24 hours of age amniotic fluid, tracheal fluid, and sheep's colostrum do not arrest respiration when introduced into the upper airway, while glucose solutions and cow's milk do. If one of these inhibitory agents remains in the upper airway, then apnoea continues, P_{aO_2} falling to fetal level and P_{aCO_2} rising in excess of 150 mm of mercury the lamb dying in 35–40 minutes.

Cheviot lambs (8) over 48 hours of age and ewes demonstrated exactly the same discrimination between water and saline as described. However they showed 'breakthrough' of respiration after only transient apnoea.

Localization experiments place the site of the receptor at the entrance to the larynx. The use of a variety of chemical solutions suggest the receptor to be a chemoreceptor, possibly a taste receptor. Superior laryngeal nerve section (bilateral) abolished the discrimination between these agents, and apnoea did not occur.

However, of 9 Dorset lambs under 24 hours of age, 8 showed 'breakthrough' breathing with water in the upper airway. These lambs all had a good response to hypoxia. Thus this strain appeared to be more mature in these aspects than young lambs of the Cheviot breed. Nevertheless, two Dorset lambs, one over 48 hours of age having shown a good hypoxic response, remained apnoeic with water in the upper airway. Therefore in 4 Dorset lambs already shown to have a good hypoxic response the carotid bodies were inactivated, removing the response to hypoxia but not affecting the response to water and saline already demonstrated.

We confirm the presence of a chemoreceptor at the entrance to the larynx; at least part of the reflex pathway is contained in the superior laryngeal nerve. There was considerable individual as well as strain variation in the response. The possible role of such a pathophysiological entity in apnoea of the newborn and so-called sudden death in infancy was discussed.

Pulmonary blood flow in newborn. Robert Dinwiddie and George Russell (*Aberdeen*). Previous workers have described the measurement of pulmonary blood flow in newborn infants using nitrous oxide as the indicator gas with a single-breath body plethysmographic technique, and using monochlorodifluoromethane ('Freon-22') with a rebreathing technique; the results obtained have correlated well with estimates of cardiac output made by conventional methods.

Using 3% nitrous oxide as the indicator gas, we have studied effective pulmonary blood flow in healthy newborn infants using a rebreathing technique. The results are similar to those obtained by other techniques (mean effective pulmonary blood flow = 167 ml/kg per min (SD 35.7); 2.80 l/m² per min (SD 0.64)). Recirculation proved to be only a theoretical problem;